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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,181	11/21/2001	Igor Gonda	AERX-088	1229

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EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/990,181	GONDA ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

An amendment was received and entered on 2/3/04.

Claim 7 was cancelled as requested.

Claims 1-6 and 8-28 are pending and under consideration in this Office Action.

Claim Objections Withdrawn

The objections set forth in the previous Action are withdrawn in view of Applicant's amendments.

Rejections Withdrawn

The rejections of claims 5, 8, 10, 27, and 28 under 35 USC 112, second paragraph are withdrawn in view of Applicant's amendments.

The rejection under 35 USC 102 over Douthart is withdrawn in view of Applicant's amendments.

The rejections of claims 16, 19, and 26 under 35 U.S.C. 103(a) as being unpatentable over Heyes et al (Nature (1974) 247 (5441): 485-487 in view of by Douthart et al (US Patent 4,400,375, issued 8/23/83), and Douthart et al (J. Interferon Research (1982) 2(4): 493-499) is withdrawn in favor of new grounds of rejection necessitated by amendment.

The rejection of claims 21-24, 27, and 28 under 35 U.S.C. 103(a) as being unpatentable over Gautam (2000), Douthart (1983), Douthart (1982), Dubensky (1983)

and Gonda et al is withdrawn in favor of new grounds of rejection necessitated by amendment.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4, 5, 8, 10-12, 15-20, 25 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al (WO 00/40692, published 7/13/00).

Wang teaches compositions comprising plasmid DNA complexed with cationic aminoglycosides, and methods of using them for delivery to cells. See e.g. claims 1 and 19 on pages 21 and 22. The cationic amino glycosides include e.g. amikacin, arbekacin, deoxydihydrostreptomycin, destomycin A, dibekacin, dihydrostreptomycin, genticin, gentamicin, hygromycin B, isepamycin, kanamycin A, kanamycin B, kanamycin C, micronomicin, paromomycin, ribostamycin, streptomycin, streptonicozid, and tobramycin. See claim 27 on page 23. The nucleic acid may encode a biologically active protein. See e.g. claim 18 on page 22. The compositions may be administered in vivo by a variety of routes including parenterally, e.g., intraarticularly, intravenously, intraperitoneally, subcutaneously, or intramuscularly, endoscopically by aerosol inhaled into the lungs, epidermally or intradermally. See pages 14 and 15. Targeting

molecules may be included. See page 12, lines 18-20. Delivery may be in vivo or in vitro. See page 6, lines 20-25.

Claim 10 is included in the rejection because, although Wang does not measure transfection efficiency, the recited improvement of transfection efficiency is considered to be inherent in the structure of the claimed composition. Because there is no apparent difference between the structure of the complexes of Wang and the instantly claimed compositions, the compositions of Wang are considered to have the same functional characteristics of the claimed compositions. Similarly, claims 15 and 18 are included because the required reduction in physical volume is considered to be inherent in the compositions. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Thus Wang anticipates the claims

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 4, 5, 8, 10-12, 15-20, 25 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al (WO 00/40692, published 7/13/00) in view of Unger et al (US Patent 5,469,854, issued 11/28/95).

Claims 1, 2, 4, 5, 8, 10-12, 15-20, 25 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al (WO 00/40692, published 7/13/00).

Wang teaches compositions comprising plasmid DNA expression vectors complexed with cationic aminoglycosides, and methods of using them for delivery to cells and expression of encoded proteins. See e.g. claims 1 and 19 on pages 21 and 22. The cationic amino glycosides include e.g. amikacin, arbekacin, deoxydihydrostreptomycin, destomycin A, dibekacin, dihydrostreptomycin, genticin, gentamicin, hygromycin B, isepamycin, kanamycin A, kanamycin B, kanamycin C, micronomicin, paromomycin, ribostamycin, streptomycin, streptonicozid, and tobramycin. See claim 27 on page 23. The nucleic acid may encode a biologically active protein. See e.g. claim 18 on page 22. The compositions may be administered in vivo by a variety of routes including parenterally, e.g., intraarticularly, intravenously, intraperitoneally, subcutaneously, or intramuscularly, endoscopically by aerosol inhaled into the lungs, epidermally or intradermally. See pages 14 and 15. Targeting

molecules may be included. See page 12, lines 18-20. Delivery may be in vivo or in vitro. See page 6, lines 20-25.

Wang does not teach cosmid or phagemid vectors.

Unger teaches that plasmids phagemids and cosmids can be used interchangeably as expression vectors. See paragraph 99 of detailed description.

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute a cosmid or a phagemid for the plasmid of Wang. MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). Furthermore, MPEP 2144.07 indicates that the selection of a known material based on its suitability for its intended use supports the determination of prima facie obviousness. See also Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945).

Claim 10 is included in the rejection because, although Wang does not measure transfection efficiency, the recited improvement of transfection efficiency is considered to be inherent in the structure of the claimed composition. Because there is no apparent difference between the structure of the complexes of Wang and the instantly claimed compositions, the compositions of Wang are considered to have the same functional characteristics of the claimed compositions. Similarly, claims 15 and 18 are included because the required reduction in physical volume is considered to be inherent

in the compositions. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Claims 6, 9, 21, 22, 27, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al (WO 00/40692, published 7/13/00) and Unger et al (US Patent 5,469,854, issued 11/28/95) as applied to claims 1, 2, 4, 5, 8, 10-12, 15-20, 25 and 26 above, and further in view of Gonda et al (US Patent 6,070,575, issued 6/6/00).

Wang and Unger can be combined to render obvious compositions comprising plasmids, phagemids, or cosmids complexed with cationic aminoglycosides, and methods of delivering them in vivo to the lung by forming an aerosol for the purpose of expressing encoded proteins in vivo.

The combined references do not explicitly teach aerosol particles having an aerodynamic diameter in a range of from about 0.5 microns to 12 microns recited in claims 6,27, and 28, or the narrower range of 2-6 microns recited in claims 9, 21, and

22. The references do not teach a method of creating an aerosol by forcing the composition through the pores of a membrane.

Gonda teaches that "aerosolized particles for respiratory delivery must have a diameter of 12 microns or less, and that "topical lung treatment can be accomplished with particles having a diameter in the range of 0.01 to 12.0 microns." See column 1, lines 12-14 and 17-19. Gonda also teaches a convenient process and apparatus for creating such aerosols, that requires forcing a composition to be aerosolized through a porous membrane. See e.g. claims 14 and 15.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use aerosol particles having an aerodynamic diameter in the range of 0.35 to 12 microns. One would have been motivated to do so because Gonda teaches that this range of particle sizes is useful for topical delivery to the lung. With regard to the narrower range of 2-6 microns recited in claim 9, MPEP 2144.05 states that "[i]n the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed.Cir. 1990).

It would have been similarly obvious to use the apparatus of Gonda to generate the aerosol because it is more efficient than devices that adjust the size of aerosol particles after aerosol generation. See paragraph bridging columns 2 and 3 of Gonda.

Thus the invention as a whole was prima facie obvious.

Claims 1-5, 8, and 10-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gautam et al (Mol. Ther. (2000) 2(4): 318-323) in view of Douthart (1983), Douthart (1982), and Dubensky et al (US Patent 5,789,245, issued 8/4/1999).

Gautam teaches a method of inhibiting experimental lung metastases by aerosol delivery to a mouse's lungs of a complex comprising a plasmid DNA encoding p53 bound to the polycation polyethyleneimine (PEI). The pH of the complexes was 7.0-7.5. See abstract, and page 319, paragraph 4.

Gautam does not teach a composition comprising a nucleic acid and a cationic aminoglycoside; or the inclusion of targeting moieties, nuclear localization peptides, or endosomolytic peptides.

Douthart (1983) discloses complexes of dsRNA with a variety of polycations including polylysine, DEAE-dextran, protamine, histone, and colistin, as well as three different cationic aminoglycosides (tobramycin, neomycin, and streptomycin). See column 1, lines 38-45. Douthart (1983) teaches that, for more efficient delivery, the cationic aminoglycoside:nucleic acid complex can be delivered in a liposome. See paragraph 32 of the brief summary. The compositions of Douthart may comprise water and have a pH of 6.8 to 7.2. See column 3, lines 32-40.

Douthart (1982) teaches that complexes between dsRNA and polycations give greater induction of interferons than naked dsRNA, and indicates that this is due to increased cellular uptake of the complexed dsRNA. See abstract and page 493, lines 3 and 4 pf paragraph bridging pages 493 and 494.

Both Douthart (1982) and Douthart (1983) teach that administration to cells of cationic aminoglycoside:dsRNA complexes results in increased interferon production. Given these teachings, one of ordinary skill in the art would deduce that cationic aminoglycosides improve interferon production by improving cellular uptake of dsRNA.

Dubensky is relied upon in this rejection for a discussion of the theory behind using polycations to facilitate nucleic acid delivery to cells. See column 79, lines 34-45, in which Dubensky indicates that polycations function to neutralize negative charges on a nucleic acid molecule and condense it into a compact form, resulting in increased transfection efficiency. One of ordinary skill in the art appreciates that eukaryotic cells generally bear a negative surface charge, so neutralization of the negative charges on nucleic acids is thought to minimize charge repulsion between nucleic acids and target cells. Dubensky also teaches that transfection complexes may be modified to include targeting moieties, nuclear localization peptides, or endosomolytic peptides. See column 79, lines 45-57.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Gautam by substituting a cationic aminoglycoside such as tobramycin for PEI, and to deliver plasmid DNA/cationic aminoglycoside complexes rather than plasmid DNA/PEI complexes. In light of the cited teachings above, one of ordinary skill in the art would consider PEI and cationic aminoglycosides to be art recognized equivalents because they both function to bind nucleic acids and facilitate uptake into cells. MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining

essential function, such elements are art-recognized equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). Furthermore, MPEP 2144.07 indicates that the selection of a known material based on its suitability for its intended use supports the determination of prima facie obviousness. See also Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945).

It would have been similarly obvious to modify the method of Gautam by including targeting moieties, nuclear localization peptides, or endosomolytic peptides in the delivery composition. One would have been motivated to do so because Dubensky teaches that these modifications facilitate the transfection process. See column 79, lines 45-57.

Claim 10 is included in the rejection because, although cited art does not measure transfection efficiency, the recited improvement of transfection efficiency is considered to be inherent in the structure of the claimed composition. Because there is no apparent difference between the structure of the complexes of cited art and the instantly claimed compositions, the compositions of cited art are considered to have the same functional characteristics of the claimed compositions. Similarly, claims 15 and 18 are included because the required reduction in physical volume is considered to be inherent in the compositions. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an Applicant to prove that the prior art products do not

necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Thus the invention as a whole was prima facie obvious.

Claims 1-5, 8, and 10-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gautam et al (Mol. Ther. (2000) 2(4): 318-323) in view of Douthart (1983), Douthart (1982), Dubensky et al (US Patent 5,789,245, issued 8/4/1999), Unger et al (US Patent 5,469,854, issued 11/28/95).

The teachings of Gautam (2000), Douthart (1983), Douthart (1982), and Dubensky (1999) are discussed in the preceding rejection. These references can be combined to render obvious compositions comprising complexes of plasmid DNA expression vectors and cationic aminoglycosides, and methods of delivering the compositions to cells in vivo.

The combined references do not teach cosmids or phagemids.

Unger teaches that plasmids phagemids and cosmids can be used interchangeably as expression vectors. See paragraph 99 of detailed description.

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute a cosmid or a phagemid for the plasmid of Gautam. MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). Furthermore, MPEP 2144.07 indicates that the selection of a known material based on its suitability for its intended use supports the determination of prima facie obviousness. See also Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945).

Thus the invention as a whole was prima facie obvious.

Claims 6, 9, 27, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gautam et al (2000), Douthart (1983), Douthart (1982), Dubensky (1999), and Unger (1995) as applied to claims 1-5, 8, and 10-26, above, and further in view of Gonda et al (US Patent 6,070,575, issued 6/6/00).

. The teachings of Gautam (2000), Douthart (1983), Douthart (1982), Dubensky, and Unger (1999) are discussed in the preceding rejection. These references can be combined to render obvious compositions comprising complexes of plasmids, phagemids, or cosmids with cationic aminoglycosides, and methods of delivering the compositions to lung cells in vivo by aerosol.

The combined references do not explicitly teach aerosol particles having an aerodynamic diameter in a range of from about 0.5 microns to 12 microns recited in claims 6,27, and 28, or the narrower range of 2-6 microns recited in claims 9, 21, and 22. The references do not teach a method of creating an aerosol by forcing the composition through the pores of a membrane.

Gonda teaches that "aerosolized particles for respiratory delivery must have a diameter of 12 microns or less, and that "topical lung treatment can be accomplished with particles having a diameter in the range of 0.01 to 12.0 microns." See column 1, lines 12-14 and 17-19. Gonda also teaches a convenient process and apparatus for creating such aerosols, that requires forcing a composition to be aerosolized through a porous membrane. See e.g. claims 14 and 15.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use aerosol particles having an aerodynamic diameter in the range of 0.35 to 12 microns. One would have been motivated to do so because Gonda teaches that this range of particle sizes is useful for topical delivery to the lung. With regard to the narrower range of 2-6 microns recited in claim 9, MPEP 2144.05 states that "[i]n the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed.Cir. 1990).

It would have been similarly obvious to use the apparatus of Gonda to generate the aerosol because it is more efficient than devices that adjust the size of aerosol particles after aerosol generation. See paragraph bridging columns 2 and 3 of Gonda.

Thus the invention as a whole was prima facie obvious.

Response to Arguments

Applicant's arguments filed 2/3/04 have been fully considered as they apply to the grounds of rejection set forth above, but they are not persuasive.

At page 9 of the response, Applicant alleges that the Gautam, Douthart (1982 and 1983), and Dubensky references do not teach DNA sequences in combination with an aminoglycoside, and alleges that it is not possible to combine the references in such a way as to suggest the presently claimed invention. In response, the PTO notes that the cited art clearly teaches plasmid DNA. Applicant's attention is directed to Gautam who teaches plasmid DNA encoding p53. This reference can be combined with the other cited references to arrive at the claimed invention for the reasons set forth in the rejection. Applicant has not addressed the motivation to combine references that was set forth by the Office. As such Applicant's arguments are unpersuasive and the rejection is maintained.

Applicant argues further that even if the cited references could be combined, the rejection would be improper because nothing in them suggests that one would expect to improve the efficiency of transfecting cells by combining DNA with a cationic aminoglycoside. This argument is unpersuasive because Wang (2000) clearly showed prior to Applicant's disclosure that delivery of plasmid DNA is improved by formation of complexes with cationic aminoglycosides. See Fig. 4. Thus one of ordinary skill in the art would clearly expect an improvement in transfection efficiency. Furthermore, both

Thus the invention as a whole was prima facie obvious.

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Applicant's arguments filed 2/3/04 have been fully considered as they apply to the grounds of rejection set forth above, but they are not persuasive.

At page 9 of the response, Applicant alleges that the Gautam, Douthart (1982 and 1983), and Dubensky references do not teach DNA sequences in combination with an aminoglycoside, and alleges that it is not possible to combine the references in such a way as to suggest the presently claimed invention. In response, the PTO notes that the cited art clearly teaches plasmid DNA. Applicant's attention is directed to Gautam who teaches plasmid DNA encoding p53. This reference can be combined with the other cited references to arrive at the claimed invention for the reasons set forth in the rejection. Applicant has not addressed the motivation to combine references that was set forth by the Office. As such Applicant's arguments are unpersuasive and the rejection is maintained.

Applicant argues further that even if the cited references could be combined, the rejection would be improper because nothing in them suggests that one would expect to improve the efficiency of transfecting cells by combining DNA with a cationic aminoglycoside. Figure 1 of the Application shows a 5.5-fold inprovement of gene expression in cells transfected with gentamicin:DNA complexes relative to naked DNA. This argument is unpersuasive because Wang (2000) clearly showed prior to Applicant's disclosure that formation of plasmid DNA complexes with a variety of

cationic aminoglycosides resulted in greater than 5.5-fold improvement in gene expression. See Fig. 4. Thus one of ordinary skill in the art would clearly expect an improvement in transfection efficiency. Furthermore, both Douthart (1982) and Douthart (1983) teach that administration to cells of cationic aminoglycoside:dsRNA complexes resulted in increased interferon production. Given these teachings, one of ordinary skill in the art would deduce that cationic aminoglycosides improve interferon production by improving cellular uptake of dsRNA. Applicant has presented no reason or logic to indicate that one would not have expected to see the same improvement for DNA:cationic aminoglycoside complexes. Finally, Dubensky indicates that polycations function to neutralize negative charges on a nucleic acid molecule and condense it into a compact form, resulting in increased transfection efficiency. Applicant has presented no reason or logic to indicate that one would not also expect cationic aminoglycosides to neutralize negative charges on a DNA and condense it into a compact form, resulting in increased transfection efficiency. For these reasons, Applicant's arguments are unpersuasive and the rejection is deemed proper.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, John Leguyader, be reached at 571-272-0760. The official central fax number is 703-872-9306. Inquiries of a general nature or relating to the status of the application should be directed to the Patent Analyst Trina Turner whose telephone number is 571-272-0564.

DAVE T. NGUYEN
PRIMARY EXAMINER

Richard Schnizer, Ph.D.